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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,697	10/05/2006	Jurgen Wagner	33714-US-PCT	2925

1095 7590 07/01/2009

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
07/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,697	WAGNER ET AL.	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 15-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 3/30/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112--previous

Claims 5 and 15 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of transplant rejection or graft-versus-host disease, does not reasonably provide enablement for prevention of graft-versus-host disease. This rejection now applies to newly amended **claims 17-19**.

The same rejection applies since the term "prophylaxis" means prevention.

Applicant is reminded that graft-versus-host disease (GVHD) is not necessarily the same as transplant rejection. As mention previously, GVHD can affect almost any organ in the body, and it often mimics autoimmune diseases such as Sjörgren's syndrome, rheumatoid arthritis, systemic lupus erythematosis and scleroderma.

Applicant is also reminded that while phrophylaxis might theoretically be possible under strictly controlled laboratory conditions, as a practical matter, it is nearly impossible to achieve in the "real world" in which patients live. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its "full scope" a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103--previous

Claims 5 and 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Heath et al. (US 5,545,636) in view of Albert et al., (US 2004/0053949), and further in view of Goekjian et al., (Expert Opinion Investigative Drugs 2001). This rejection also applies to newly amended **claims 16-19**.

Applicants do not concede that Heath suggests the compounds recited in the pending claims. However, applicant is reminded that Heath is relied on in the specification in regard to the synthesis of the instant compounds (see specification at pg. 8, third paragraph).

Applicant argues that without some indication that organ or tissue transplant rejection, graft-verus-host disease or prolongation of graft survival would benefit from such PKC beta isozyme specificity, one skilled in the art, upon reading Heath, simply would not select such a compound for treatment or prophylaxis thereof. However, applicant is again reminded that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." KSR v. Teleflex, 127 S.Ct. 1727, 1742 (2007). Heath teaches that its compounds are isozyme selective inhibitors of beta-1 and beta-2 isozymes of PKC. Graft-versus-host disease (GVHD) is recognized in the prior art as a PKC-linked immunodisorder.[1] Goekjian et al. teaches the use of a compound with selective inhibition for beta-1 and beta-2 isozymes of PKC, Ro 32-0432, for treating graft-versus-host response models in rats (see Goekjian et al. at pg. 2131, left column,

2nd paragraph; see also Table 4, at pg. 2128 for relation to isozymses of PKC). Ro 31-0432 has also been compared to indolocarbozoles, which are of the same class as the compounds of Heath and Albert (see Goekjian et al., section 3.3, at pg 2131).

Furthermore, Albert teaches indolylmaleimide derivatives that inhibit PKC beta isoforms (see paragraph [0221]), and are useful in the treatment and/or prevention of T-cell mediated acute or chronic inflammatory diseases or disorders, autoimmune diseases, graft rejection or cancer" (see Abstract). Since the compounds of Heath are indolymaleimide derivatives that inhibit PKC beta isoforms and are useful in treating inflammation and autoimmune disorders, the artisan would reasonably expect these compounds to also be useful in treating graft rejection. (Compare diseases treated in Heath at col.11, lines 60-67 with diseases treated in Albert at paragraph [0245].) The artisan would reasonably infer that the compounds of Heath are useful for treating other PKC mediated diseases indicated in Albert, based on their similar structure and function with the compounds of Albert.

In regard to applicant's insistence that only PKC alpha inhibitors are known to be useful of treating graft survival, the Examiner would like to point out that the compounds of Albert and the Ro 32-0432 of Goekjian inhibit **beta** isoforms as well (see discussion above). The Examiner would also add that applicant's claimed compound also inhibits the PKC alpha isoform. For evidentiary purposes, the examiner cites Graff et al., (Cancer Research 2005). At Table 1, Graff et al. shows that LY317615 (Enzasturin) inhibits the alpha, gamma, and epsilon isoforms of PKC (see Table 1 at pg. 7464; see

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[1] Hong Hu, "Recent discovery and development of selective protein kinase C inhibitors." Drug Discovery Today

also instant specification at pg. 8, second paragraph for LY 317615, also referred to as Compound A).

Since the prior art has shown that compounds with the same isozyme selectivity for PKC are useful for treating GVHD and graft survival, the artisan would have reasonably concluded that the compounds of Heath would be useful in treating GVHD and graft survival, as well.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

1996:1(10); at pg 445, right column, 1st paragraph.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612